

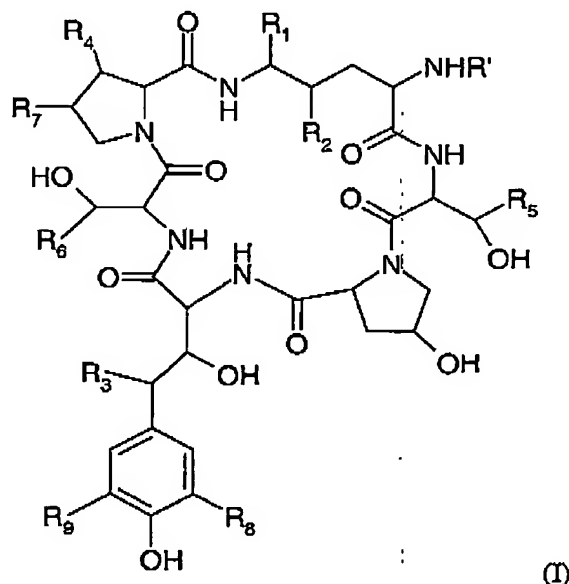
Application Ser. No.: 10/031,764  
 Filing Date: September 30, 2002  
 Examiner: Audet, Maury A.

**Amendment Pursuant to 37 C.F.R. § 1.121**

**IN THE CLAIMS:**

The claims set forth below with amendments as indicated will replace all prior versions and listing of claims in the application.

1. (currently amended) A compound selected from the group consisting of a cyclohexapeptide compound of the formula (I)



wherein,

R' is selected from the group consisting of C<sub>9</sub>-C<sub>20</sub> alkyl; C<sub>9</sub>-C<sub>20</sub> alkenyl; C<sub>9</sub>-C<sub>20</sub> alkoxyphenyl, phenyl, biphenyl, terphenyl, and naphthyl; C<sub>1</sub>-C<sub>12</sub> alkylphenyl, C<sub>8</sub>-C<sub>12</sub> alkenylphenyl, C<sub>1</sub>-C<sub>12</sub> alkoxyphenyl; linoleoyl; palmitoyl; 12-methylmyristoyl; 10,12-dimethylmyristoyl; and COC<sub>6</sub>H<sub>4</sub>(p)OC<sub>8</sub>H<sub>17</sub>,

R<sub>1</sub> is selected from the group consisting of -CN; -CH<sub>2</sub>NH<sub>2</sub>; -N<sub>3</sub>; aryl; substituted aryl; imidazolyl; morpholinoethylamino; -OR, wherein R is C<sub>1</sub>-C<sub>12</sub> alkyl, substituted alkyl of (CH<sub>2</sub>)<sub>n</sub>-X, where n is 1-5 and X is selected from the group

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consisting of OH, aryl, Cl, Br, I, COOY and CN, wherein Y is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>12</sub> alkenyl, aryl, fused aryl, substituted aryl, a heterocyclic containing 1-3 heteroatoms, mono or di-substituted aminoalkyl and a hydroxy protecting group;

R<sub>3</sub> is selected from the group consisting of -OH; -CN; -CH<sub>2</sub>NH<sub>2</sub>; -N<sub>3</sub>; aryl; substituted aryl; heterocyclyl and substituted heterocyclyl with 1-3 of heteroatoms; aminoalkylamino; mono or di-substituted linear or cyclic aminoalkylamino; imidazolyl; -OR, wherein R<sub>4</sub> is C<sub>1</sub>-C<sub>12</sub> alkyl; substituted alkyl of (CH<sub>2</sub>)<sub>n</sub>-X, where n is 1-5 and X is selected from the group consisting of OH, aryl, Cl, Br, I, COOY, CN, NH<sub>2</sub> and heterocyclic, wherein Y is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>12</sub> alkenyl, aryl, fused aryl, substituted aryl, a heterocyclic containing 1-3 heteroatoms, mono or di-substituted aminoalkyl, and a hydroxy protecting group;

R<sub>2</sub> and R<sub>4</sub> are independently -H or -OH;

R<sub>5</sub> is -H or -CH<sub>3</sub>;

R<sub>6</sub> is selected from the group consisting of -H; -CH<sub>3</sub> and -CH<sub>2</sub>CONH<sub>2</sub>;

R<sub>7</sub> is selected from the group consisting of -H; -CH<sub>3</sub> and -OH;

R<sub>8</sub> and R<sub>9</sub> are independently -H or -CH<sub>2</sub>-Sec. amine in which the sec. amine is attached to -CH<sub>2</sub> through its N linkage; with the proviso that both R<sub>8</sub> and R<sub>9</sub> are not simultaneously hydrogen and wherein the secondary amine is selected from the group consisting of piperidine, pyrrolidine, 4-methylpiperidine, morpholine, dimethylamine, diisopropylamine, 4-piperidino-piperidine, piperazine, 1-methylpiperazine, 1-(2-fluorophenyl)piperazine, 1-(2-chlorophenyl)piperazine,

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1-(2-pyrimidyl)piperazine, 1-(4-fluorophenyl)piperazine, N-( $\alpha,\alpha,\alpha$ -trifluoro-m-tolyl)piperazine, 1-phenylpiperazine, 1-benzylpiperazine, 1-(2-pyridyl)piperazine, 1-(4-pyridyl)piperazine, 1-(4-methylphenyl)piperazine, 1-(2,6-dimethylphenyl)piperazine, 1-(1-phenylethyl)piperazine, dibenzylamine, N-(tertbutyl)benzylamine and N-(isopropyl)-benzylamine;  
and its non-toxic pharmaceutically acceptable salts.

2. (previously presented) The compound of claim 1 wherein  $R_1$  is OR, and  $R_3$  is selected from the group consisting of -OH, -OR and imidazolyl wherein R in each case is selected from the group consisting of  $C_1$ - $C_{12}$  alkyl, substituted alkyl of  $-(CH_2)_n-X$ , where n is 1-5, X is selected from the group consisting of OH, aryl, Cl, Br, I, COOY and CN, and wherein Y is selected from the group consisting of  $C_1$ - $C_6$  alkyl,  $-C_2$ - $C_{12}$ -alkenyl, aryl, fused aryl, substituted aryl, a heteroaryl containing 1-3 heteroatoms, a heterocyclic containing 1-3 heteroatoms, mono or di-substituted aminoalkyl and a hydroxy protecting group.
3. (previously presented) The compound of claim 1 wherein  $R'$  is selected from the group consisting of linoleoyl, palmitoyl, 12-methylmyristoyl, 10,12-dimethylmyristoyl and  $-COC_6H_4(p)OC_8H_{17}$ .
4. - 5. (canceled)
6. (previously presented) The compound of claim 1, wherein  $R'$  is 12-methylmyristoyl,  $R_1$  is selected from the group consisting of -CN,  $-CH_2NH_2$ ,  $-N_3$ , aryl, substituted aryl,  $-OCH_2C_6H_4$ ,  $-OCH_3$ ,  $-OCH_2OH$ , morpholinoethylamino and imidazolyl  $R_3$  is selected from the group consisting of -OH, -CN,  $-CH_2NH_2$ ,  $-N_3$ , aryl, substituted aryl, heterocyclyl and substituted heterocyclyl having 1-3 heteroatoms, aminoalkylamino, and mono or di-substituted linear or cyclic aminoalkylamino,  $R_5$  and  $R_7$  are both  $-CH_3$ ; and  $R_6$  is -H.

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7. (original) An antifungal composition comprising a fungicidally effective amount of a compound of claim 1, and a non-toxic pharmaceutically acceptable carrier.

8. cancelled.

9. (previously presented) A process for the production of a compound of claim 1 comprising:

- a) reacting a cyclohexapeptide compound of claim 1, wherein R', R<sub>2</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub> and R<sub>7</sub> are as defined in claim 1, R<sub>1</sub> and R<sub>3</sub> are both -OH, and R<sub>8</sub> and R<sub>9</sub> are -H, with an alcohol in the presence of an acid in an aprotic solvent at a temperature of 0°C to 60°C to obtain the corresponding cyclohexapeptide derivative of claim 1 wherein R', R<sub>2</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub> and R<sub>7</sub> are as defined in claim 1, R<sub>1</sub> and R<sub>3</sub> are independently -OH or -OR wherein at least one of R<sub>1</sub> or R<sub>3</sub> is -OR, R is selected from the group consisting of C<sub>1</sub>-C<sub>12</sub> alkyl, C<sub>2</sub>-C<sub>12</sub> alkenyl, fused aryl, substituted aryl, a heterocyclyl containing 1-3 heteroatoms, mono or di-substituted aminoalkyl; and a hydroxy protecting group, and R<sub>8</sub> and R<sub>9</sub> are -H;
- b) reacting the compound of step (a) with a secondary amine in the presence of paraformaldehyde in an aprotic solvent at a temperature of 60°C to 150°C to obtain the desired compound of formula I, isolating and purifying the resulting compound from the reaction mixture in a known manner and optionally converting the compound of formula I into its pharmaceutically acceptable salt in a known manner.

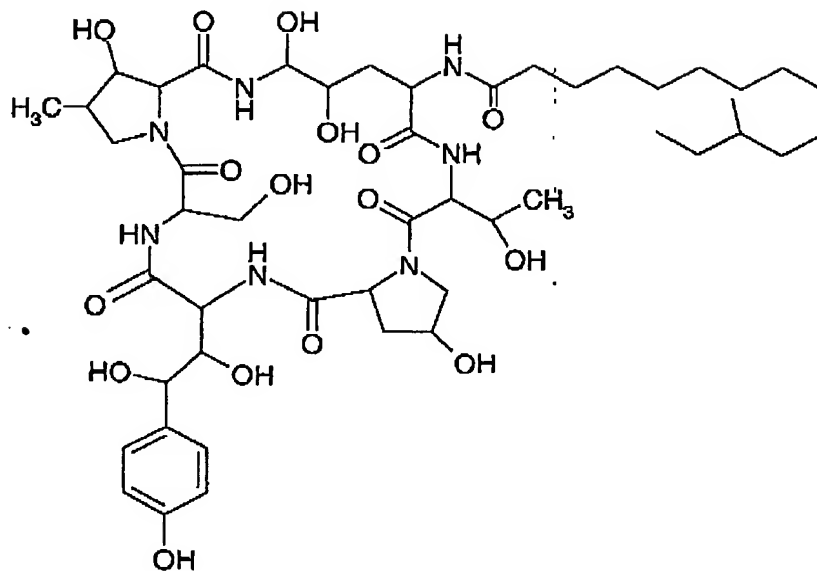
10. (previously presented) A process for the preparation of a cyclohexapeptide compound of claim 1 comprising:

- a) reacting mulundocandin of the formula

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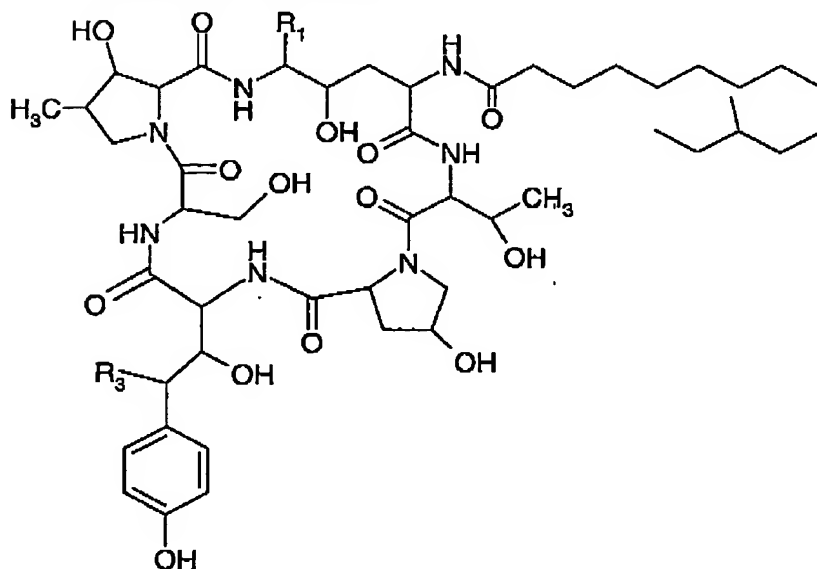
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(IV)

with a nucleophile in the presence of an acid in an aprotic solvent at a temperature of 0°C to 60°C to obtain the corresponding cyclohexapeptide derivative of the formula



(V)

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wherein  $R_1$  and  $R_3$  are  $-OH$  or  $-SR$  with at least one of  $R_1$  or  $R_3$  is  $-SR$ ,  $R$  is selected from the group consisting of  $C_1$ - $C_{12}$  alkyl, substituted alkyl of  $-(CH_2)_n-X$ , where  $n$  is 1-5,  $X$  is  $Cl$ ,  $Br$ ,  $I$ ,  $COOY$ ,  $CN$ ,  $NH_2$  and a heterocyclic,  $Y$  is selected from the group consisting of  $C_1$ - $C_6$  alkyl;  $C_2$ - $C_{12}$  alkenyl; aryl; fused aryl; substituted aryl; a heterocyclyl containing 1-3 heteroatoms; mono or di-substituted aminoalkyl; and a hydroxy protecting group;

- b) reacting the compound of step (a) with an oxidizing agent in an aqueous medium at a temperature of  $20^\circ C$  to  $60^\circ C$  to obtain the corresponding sulfones of formula V wherein  $R_1$  and  $R_3$  are  $-OH$  or  $-S(O_2)R$ , with at least one of  $R_1$  or  $R_3$  is  $-SO_2R$ ,  $R$  is selected from the group consisting of  $C_1$ - $C_{12}$  alkyl, substituted alkyl of  $-(CH_2)_n-X$ , where  $n$  is 1-5,  $X$  is  $Cl$ ,  $Br$ ,  $I$ ,  $COOY$ ,  $CN$ ,  $NH_2$  and a heterocyclic,  $Y$  is selected from the group consisting of  $C_1$ - $C_6$  alkyl;  $C_2$ - $C_{12}$  alkenyl; aryl; fused aryl; substituted aryl; a heterocyclyl containing 1-3 heteroatoms; mono or di-substituted aminoalkyl; and a hydroxy protecting group;
- c) reacting the sulfone of step(b) with a secondary amine in a solvent at a temperature of  $20^\circ C$  to  $60^\circ C$  to obtain the desired compound of claim 1, isolating and purifying the resulting compound and optionally converting the compound of claim 1 into its pharmaceutically acceptable salt in a known manner.